REMARKS

This is in response to the Action mailed August 3, 2007.

Claim 1 is amended in order to specify that the recited method is used to treat a mammary or pancreatic carcinoma, or to treat pemphigus vulgaris. Support is in, *e.g.*, original claims 6 and 7, which are canceled without prejudice. New claim 19 is added to specify that the recited method is used to treat pemphigus vulgaris. Support is in, *e.g.*, original claim 7.

35 USC §112, first paragraph

Reconsideration and withdrawal of the rejection of claims 1-13 under the first paragraph of 35 USC §112 for lack of enablement are respectfully requested. The Examiner's position is believed to be that there are many types of tumors, but the specification does not suggest that any reasonable number of tumors could be treated with the present methods. Applicant respectfully traverses. First, claim 1 does not recite the treatment of any and all tumors, but rather the treatment or prevention of a urokinase-associated or urokinase receptor-associated disease. Further, by virtue of the present amendment, claim 1 now recites that the method is used to treat a mammary or pancreatic carcinoma, or to treat pemphigus vulgaris. Indeed, because pemphigus vulgaris is not a cancer, no reason at all is given in the pending Action as to why treatment of such disease would not be enabled. Therefore, it is believed that claims 1-13 and 19 are enabled.

35 USC §103

Reconsideration and withdrawal of the rejection of claims 14-18 under 35 USC §103 as being unpatentable over the combination of WO 92/08709 and WO 00/17158 are respectfully requested.

The compounds disclosed in WO '158 are quite different from the compounds recited in present claims 1-13. The WO '158 compounds are all amidino compounds (*i.e.*, they all have the C(NH)(NH_2) substituent on the phenyl ring), whereas the presently claimed compounds are all guanidino compounds having the NH-C(NH)NH_2 substituent on the phenyl ring. Even with WO '158 in hand, one of ordinary skill would not be led to substitute a guanidino group for an amidino group. There is no suggestion from the references that one would expect guanidino compounds to be urokinase inhibitors from the mere fact that amidino compounds are urokinase inhibitors, and both amidino and guanidino compounds inhibit thrombosis. WO '158 suggests many variables in other portions of the molecule, but all of the compounds contain the amidino group, with no suggestion of variation at that point. It is respectfully submitted that it is only in hindsight with the benefit of the present applicant's specification can it be said to be obvious to modify the WO '158 compounds as posited. Moreover, even if there were motivation in the art to make that change, one would still not have the necessary expectation of success after the modification was made. The references relied on do not provide any structure/activity link between amidino and guanidine groups in the context of inhibiting urokinase activity.

Moreover, even if the combination of references made out a *prima facie* case of obviousness (which they do not), compounds according to the present claims exhibit a surprisingly high selectivity for urokinase compared to plasmin and thrombin. The Examiner's attention is respectfully directed to the Sperl Declaration submitted September 5, 2007. There, Dr. Sperl determined the *in-vitro* inhibition of urokinase, plasmin and thrombin by two compounds according to the present invention. They were both highly selective for urokinase, as compared to plasmin and thrombin (Dec. at ¶ 4). Dr. Sperl contrasts those data with the data in the Pentapharm Product Catalog 1998 for 3-amidino

compounds. He concludes, based on the published data for those compounds, that they are much less selective for urokinase compared to plasmin and thrombin (Dec. at ¶ 5). Dr. Sperl also concludes that the high selectivity of the presently-claimed guanidine compounds is surprising and unexpected (*Id.*).

In the current Action, applicant's arguments made in the July 9, 2007 Response (prior to the availability of the Sperl Declaration) are discounted because the data were not generated side-by-side. Applicant respectfully submits that such is not a good basis for discounting those data. The Examiner has cited no precedent or rule requiring data to be generated in that manner. Moreover, the Examiner has not provided any reason to doubt the reliability of the two sets of data. Further, now that those data are presented in the Sperl Declaration, there is no good reason not to give them full weight. Dr. Sperl, who is a Ph.D. chemist and who works in the industry, obviously had no difficulty in concluding that the compounds of the present invention were much more selective.

So as to remove any possible doubt, applicant states that Dr. Sperl has run a set of experiments in parallel in which Ki measurements were made on the two compounds according to the present invention in the Sperl Declaration (WX-682 and WX-684) as well as the Pefabloc® uPA compound from the Pentapharm Product Catalog 1998. The following results were obtained:

Compound	uPA [µM]	Plasmin [µM]	Thrombin [µM]
WX-682	0.39	5.16	9.4
WX-684	0.93	4.04	25.2
Pefabloc® uPA	0.65	1.46	0.5

The compounds of the present invention were more highly selective for urokinase as compared to plasmin and thrombin than was the Pentapharm compound.[1] It is respectfully submitted that one of ordinary skill would find the high selectivity of the guanidino compounds surprising and unexpected.

Thus, for all of the foregoing reasons, the rejection should not be maintained. It is believed that the present case is in condition for allowance, and a favorable Action is respectfully requested.

Respectfully submitted,

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[1] Applicant expects shortly to submit these data in a formal declaration under Rule 132.